Abstract

Statement of the Problem:
Solid-state micropores have emerged as promising platforms for label-free detection and characterization of single particles and microorganisms. However, the weak ionic current blockade signals generated during particle translocation are often obscured by electronic noise, limiting detection sensitivity and species discrimination. Although increasing the micropore bias voltage enhances the translocation signal amplitude, the resulting increase in baseline ionic current causes saturation of high gain transimpedance amplifiers, preventing operation at the optimal sensing conditions. Therefore, there is a need for a readout architecture that enables high-bias operation while preserving low-noise performance and high transimpedance gain.

Methodology:
A DC feedback compensation-based readout architecture incorporating a low-noise baseline current cancellation path was developed to suppress the large steady-state ionic current while preserving transient translocation events. The proposed compensation technique enables operation at elevated micropore bias voltages without saturating the front-end amplifier. The readout circuit was designed to achieve a transimpedance gain of 160 dBΩ, a bandwidth of 30 kHz, and an input-referred RMS noise of 6.3 pA. Experimental validation was performed using solid-state micropores with polystyrene beads and *Escherichia coli* bacteria to evaluate sensing performance under compensated and uncompensated operating conditions.

Findings:
The proposed compensation architecture effectively suppresses the baseline ionic current, allowing stable operation at higher micropore bias voltages while maintaining low electronic noise. Experimental results demonstrate increased translocation event rates, larger ionic current blockade amplitudes, and an approximately 15.9 dB improvement in signal-to-noise ratio at a 200 mV bias compared with conventional uncompensated readout circuits. Furthermore, measurements obtained using polystyrene beads and *E. coli* bacteria exhibit distinct translocation signatures, enabling reliable discrimination of mixed particle populations.

Conclusion & Significance:
The proposed DC-compensated readout architecture significantly improves the sensitivity and throughput of solid-state micropore sensing by enabling high-bias operation without amplifier saturation. The enhanced signal-to-noise ratio and reliable differentiation of biological and synthetic particles demonstrate its potential for label-free biosensing, microorganism detection, and future nanopore-based diagnostic and analytical applications.

References

1. H. Bayley and C. R. Martin, "Resistive-pulse sensing—from microbes to molecules," *Chemical Reviews*, vol. 100, no. 7, pp. 2575–2594, 2000.
2. J. Li, M. Gershow, D. Stein, E. Brandin, and J. A. Golovchenko, "DNA molecules and configurations in a solid-state nanopore microscope," *Nature Materials*, vol. 2, no. 9, pp. 611–615, 2003.
3. C. Dekker, "Solid-state nanopores," *Nature Nanotechnology*, vol. 2, no. 4, pp. 209–215, 2007.
4. S. Howorka and Z. Siwy, "Nanopore analytics: sensing of single molecules," *Chemical Society Reviews*, vol. 38, no. 8, pp. 2360–2384, 2009.
5. A. Fragasso, C. Schmid, and A. Dekker, "Comparing current noise in biological and solid-state nanopores," *ACS Nano*, vol. 14, no. 2, pp. 1338–1349, 2020.
6. B. Veerappan and J. B. Klauda, "Nanopore sensors for biomolecular detection and characterization," *Sensors*, vol. 21, no. 15, 2021.

Biography

K. Ashoka Deepthi received the B.Tech. degree in Electronics and Communication Engineering (ECE) from the Indian Institute of Information Technology (IIIT), Nuzvid, Andhra Pradesh, India, in 2023. She is currently pursuing the Ph.D. degree with the Department of Electronic Systems Engineering, Indian Institute of Science (IISc), Bengaluru, Karnataka, India. Her research focuses on the development of solid-state nanopore-based deoxyribonucleic acid (DNA) sequencing technology. Her research interests include low-noise analog and mixed-signal integrated circuits, CMOS biosensor interfaces, transimpedance amplifier design, nanopore readout electronics, and high-sensitivity bioelectronic sensing systems.

About Institution

The Indian Institute of Science (IISc), Bengaluru, Karnataka, India, is India's premier institution for advanced scientific and technological research and higher education. Established in 1909, IISc is internationally recognized for its excellence in research across engineering, science, and interdisciplinary domains. The Department of Electronic Systems Engineering (DESE) conducts cutting-edge research in analog and mixed-signal integrated circuits, VLSI systems, semiconductor devices, embedded systems, communication systems, biomedical electronics, and sensor interface technologies. The department provides state-of-the-art research facilities and fosters innovation in developing next-generation electronic systems for healthcare, communication, and sensing applications.